UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,721	11/19/2001	David Botstein	P2730P1C55	2434

35489 7590 05/10/2006

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/989,721
Filing Date: November 14, 2001
Appellant(s): BOTSTEIN ET AL.

Daphne Reddy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/23/2006 appealing from the Office action mailed 2/23/2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

In addition to the antibody and protein acid cases disclosed by Appellants, the Examiner notes that there are a multitude of applications that are also in prosecution or under appeal that are drawn to different protein or nucleic acid sequence, but involve the same issues on appeal with regard to 35 U.S.C. §101 and §112, first paragraph (enablement); for example, see 09/904766 and 10/145124.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final filed concurrently with the Appeal Brief has been entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct.

The rejection under 35 U.S.C. §112, first paragraph for lack of adequate written description has been withdrawn.

The rejection under 35 U.S.C. §102(b) over Hillier et al. is applied only to claims 124, 129-131 and 135-138 (not to cancelled claims).

(7) Claims Appendix

A correct copy of appealed claims 124, 129-131 and 135-138 appears on page 19 of the Appendix to the appellant's brief.

(8) Evidence Relied Upon

Sen, 2000, Curr. Opin. Oncol. 12:82-88.

Hu et al., 2003, Journal of Proteome Research 2:405-412.

Hillier et al., Locus H74302, WashUMerck EST project (1995).

(9) Grounds of Rejection

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 124, 129-131 and 135-138 are rejected under §35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

The specification discloses a protein designated PRO809, and nucleic acid encoding such. There is no discussion of the structure of the protein encoded by the claimed nucleic acids, nor disclosure of any relationship between such structure and a purported function. There is no disclosure of any disease or condition in any way related to the nucleic acids that are claimed, nor disclosure of any diagnostic or analytical assay that could be performed using the claimed nucleic acids.

The specification discloses that the claimed nucleic acids may be used as hybridization probes, to make antisense nucleic acids, and for the preparation of protein, to make transgenic animals, and in gene therapy. None of these assertions is specific, as none makes use of any

specific property of the claimed nucleic acids, but rather could be asserted as a use for any nucleic acid that encodes any protein.

Utility must be in readily available form. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the protein identified in the specification as PRO809 protein or the polynucleotides encoding it, the claimed invention is incomplete. Merely using the polynucleotides to determine the properties of the encoded protein does not constitute a patentable utility.

It is further noted that PRO809 is disclosed as having given positive results in a single assay, Example 170 beginning at page 539 of the specification, a gene amplification assay. Therein, PRO809 was found to be amplified approximately two fold in 3 of 10 human lung tumor squamous cell carcinoma cell lines, 2 of 9 human lung tumor adenocarcinoma cell lines, and the sole human lung tumor large cell carcinoma cell line. The finding that the nucleic acid encoding PRO809 is amplified, likely indicating aneuploidy, in the aforementioned tumor types is insufficient to confer utility to the nucleic acid. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid. Such aneuploidy is not diagnostic of cancer, and even if it were, has not been shown to be associated with cancer in a consistent fashion. In this case, the sequence of PRO809 was found at no more than two copies per cell,

and only in a minority of tumors tested. The person of ordinary skill in the art would not consider the results to be significant or diagnostic in view of the review by Sen.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 124, 129-131 and 135-138 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

> The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 124, 129-131 and 135-138 remain rejected under 35 U.S.C. 102(b) as being anticipated by clone H74302, isolated by L. Hillier et al., WashUMerck EST Project 1995. By applicants admission at page 454 of the specification , the clone that was sequenced and designated DNA57836-1338 or PRO809, was purchased from Merck under clone designation H74302. According to NCBI, the cDNA was double stranded, and inserted in the "Lafmid BA vector", which was propagated in E. coli cells. With respect to claim 136, the DNA would necessarily have been "operably linked" to sequences in the vector for control of replication of the vector.

(10) Response to Argument

All arguments pertaining to the written description rejection are moot and will not be addressed.

At page 4 of the Brief, appellants assert that an amplification of 2-3 fold in different lung primary tumors is significant, and refer to a declaration by Dr. Goddard in support of the assertion. This argument has been fully considered but is not deemed persuasive. The Examiner notes that the 2-3 fold amplification was found in a small minority of the cell lines tested: genomic PRO809 DNA was found to be amplified approximately two-fold in 3 of 10 human lung tumor squamous cell carcinoma cell lines, 2 of 9 human lung tumor adenocarcinoma cell lines, and the sole human lung tumor large cell carcinoma cell line. No causality has been established, i.e. there is no link between the increased genomic DNA and the development of any cancer. As stated in the rejection above, and evidenced by the Sen reference, the most parsimonious explanation for the observed result is aneuploidy.

The declaration under 37 C.F.R. §1.132 by Dr. Goddard has been fully considered as follows:

In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993).

Affidavits or declarations are provided as evidence and must set forth facts, not merely conclusions. In re Pike and Morris, 84 USPQ 235 (CCPA 1949).

Dr. Goddard states at paragraph 7 that "It is my personal experience that the quantitative TaqMan PCR technique is technically sensitive enough to detect at least a 2-fold increase in gene copy number relative to control. It is further my considered scientific opinion that an at least 2-fold increase in gene copy number in a tumor tissue sample relative to a normal (i.e. a non-tumor) sample is significant and useful..." This has been fully considered but is not deemed

persuasive, as the issue, as presented in the rejection above is *not* whether the technique is sensitive enough to detect a two-fold difference in amount of DNA, but rather that such was detected in only a minority of the tested lines of human lung tumor cell lines, which increase is likely to be due to aneuploidy in the tumorous tissue, and is not diagnostic of cancer, nor evidence of overexpression, which is the actual presence of extra protein encoded *by* the nucleic acid. It remains that the sequence of PRO809 was found at no more than two copies per cell, and only in a minority of tumors tested. The person of ordinary skill in the art would not consider the results to be significant or diagnostic in view of the review by Sen. Declarant's statement of opinion regarding the significance of a two-fold increase has been considered but is not deemed persuasive, as it is not supported by fact or evidence, but rather is merely conclusory in nature, and is also not supported by the art. Sen has been previously discussed. Furthermore, the Declaration does not provide data such that the examiner can independently draw conclusions. Only Doctor Goddard's conclusions are provided in the declaration. Finally, it is noted that Dr. Goddard is an inventor in this case, and therefore has an interest in the outcome. Considering all the points above, the Goddard declaration is insufficient to establish the PRO809 is useful as a marker for the diagnosis of cancer.

Beginning at the bottom of page 4, appellants argue that "the art exemplified by the Hittelman *et al.* reference and Sen *et al.*, supports the Appellants position that, whether aneuploidy is a feature of cancerous, pre-cancerous or damaged tissue, it still provides utility for the PRO809 gene as a marker of "increased cancer risk. This argument has been fully considered but is not deemed persuasive. First, the Examiner notes that the "Hittleman" reference has not been brought forth on the record in a timely fashion for individual analysis by the examiner. Accordingly, it has not been considered and is not found to constitute evidence against the rejection. However, it remains that the PRO809 genomic amplification was minimal, and that the most parsimonious explanation is aneuploidy, with no evidence that the chromosome bearing PRO809 was preferentially amplified (as opposed to other chromosomes). Aneuploidy is also a feature of damaged tissue, and is commonly found in lung tissues, which are subject to constant environmental damage. It does not invariably or inevitably or even frequently lead to cancer; rather, such damaged cells are generally removed by the body; the development of cancer is the exception, as evidenced by the fact that the general population is constantly

suffering damage to lung cells via air pollution, whereas lung cancer remains relatively rare. Merely because amplification *may* be an *initial* step in the formation of cancer does not equate with a substantial assertion of diagnostic utility. Finally, it is noted that appellants are shifting their assertion of utility from diagnosis of cancer to diagnosis of *increased risk* of cancer. The specification does not disclose this as a utility. Further, the simple finding that the chromosome which includes the gene for PRO809 may be found to be aneuploid in *cancer cell lines* as compared to normal lung cells does *not* support the assertion that one could look for such aneuploidy as a means for determining increased risk of cancer. All the specification states is that the copy number of PRO809 was increased relative to normal tissue. It is not known what criteria appellants used for "normal", nor is there any showing of at what stage in the process of cancer genesis the gene becomes aneuploid, nor whether aneuploidy of that particular chromosome is causally associated with development of cancer. In fact, appellants argument supports the Examiner's assertion that the mere finding that a minority of tested cancer cell lines have a minimal amplification of PRO809 DNA is not sufficient to support as substantial an assertion of diagnostic utility; in order to use PRO809 as a prognosticator of increased cancer risk, one would have to know that aneuploidy of *that* chromosome is not "normal" lung damage, but rather the specific type of damage that would lead to an increased incidence of cancer.

Appellants argument that the Hu reference is not pertinent is addressed below.

Appellants argument of the art rejection at page 6 will be fully addressed below.

At pages 7-10 appellants discuss the legal standard of utility and some of the applicable case law. The Examiner finds no need to comment.

Beginning at page 10, appellants review the data presented in the specification. It is noted that Table 9 appears not at page 539, but at pages 550-554. It is further noted that the "negative control" disclosed at page 539 lines 27-29 merely states that DNA was isolated from "the cells" of "normal healthy individuals" and "pooled and used as a control". Upon re-reading the cited portion of the specification the Examiner notes that it would appear that a single pooled group of cells was used as a control, and that the specification does not disclose what *types* of cells were used. To conclude that there was an increased amount of PRO809 DNA in the cancer cells, one would have to compare to normal cells of the *same cell type*, which apparently has not been done. Appellants go on to argue that finding of 2-3 fold (the Examiner does not believe that the

data support reporting results to three decimal points) in primary lung tumors indicates that it is more likely than not the PRO809 is useful as a diagnostic tool for "detecting certain lung tumors". This argument has been fully considered but is not deemed persuasive because , as stated in the first office action on the merits, PRO809 was found to be amplified in only 3 of 10 human lung tumor squamous cell carcinoma cell lines, 2 of 9 human lung tumor adenocarcinoma cell lines, and the sole human lung tumor large cell carcinoma cell line. The data were not corrected for aneuploidy, and it is not clear or even likely that a proper (same cell type) control was used. Accordingly, even *if, in arguendo,* the data were representative and correct, amplification would only have been found in a minority of the cell lines tested; it is not clear how appellants jump from this result, which, as argued above, likely represents aneuploidy, which is commonly found in damaged (but not necessarily cancerous or precancerous) cells, to the conclusion that it is "more likely than not" that amplification of PRO809 could be used as a diagnostic measure of cancer. It is further noted that basing the conclusion that PRO809 is a cancer diagnostic on the supposed amplification in a minority of tumor cells tested without comparison to a tissue-matched "normal" control, nor to cells from normal lung epithelium (exposed to environmental damage), is not logical. If one has only looked at lung tumor cells, and not at normal tissue matched controls (as opposed to a "pooled" control of unknown origin), and concluded that because a minority of those cancers are aneuploid for PRO809 (or otherwise show a 2-3 fold amplification of the genomic DNA) that amplification of PRO809 is diagnostic of cancer, such a conclusion is similar to concluding that because some trees are green, all green things must be trees; however, it is noted that a higher proportion of trees are green than cancer cells tested for PRO809 showed amplification.

At pages 11-12, appellants once again argue that the Goddard declaration is sufficient to establish that the amplification of PRO809 by 2-3 fold in a minority of cancer cell lines tested is sufficient to establish utility of PRO809 as a diagnostic marker. The Goddard declaration has been fully considered above.

At p. 12 of the Brief, Appellant argues that some tumor markers are useful for identifying rare malignancies, and that such markers have great value in tumor diagnosis, and consequently in tumor prognosis. It would appear that appellant is arguing that because PRO809 was amplified only in a small minority of tested lung cancers (although the significance of the data

are questionable for reasons cited above) that it is therefore useful as a marker of rare malignancies and as a prognostic marker. This argument has been fully considered but is not deemed persuasive because (a) there is not sufficient evidence that PRO809 is significantly associated with either the incidence or prognosis of cancer, (b) there is no evidence of record that the types of cancers tested are not rare cancers, thus the argument that PRO809 can be used for diagnosis of rare cancers is not supported, and (c) there is no link established on the record between the use of a gene for *diagnosis* and the use of the same gene for *prognosis*. While it is true that there exist *some* markers the levels of which are both diagnostic and prognostic, there is no necessary link between the two- prognosis is prediction of the course of the disease. Since there has been no nexus established between amplification of PRO809 and the disease *process* there is clearly no support for the assertion that PRO809 has prognostic utility being a substantial assertion of utility. Further, even if the Board were to find that such met the requirements of 35 U.S.C. §101, it would require undue experimentation to perform the types of medical studies needed to use PRO809 as a prognostic; such would require studies in which the amplification of PRO809 were measure in a significant number of cancer patients over time, and trying to correlate the levels of amplification with disease state and/or patient outcome. As for the assertion that PRO809 has diagnostic utility, the Examiner considers that experimentation, which is merely invited by the specification, to constitute part of the invention itself, such experimentation being of the type not permissible under 35 U.S.C. §101, or at the very least, to be undue. In either case, all the specification has presented is the germ of an idea that PRO809 might have diagnostic utility, based upon a low level of amplification, consistent with aneuploidy, in a minority of tumor samples, as compared to an ill-characterized "pooled", non tissue matched control. Such a germ of an idea requires substantial further experimentation to determine whether the "hunch" that there is a correlation is a reality, to determine the significance of such a correlation if it exists, and then to develop methods of using PRO809 based upon such findings.

Bridging pages 12-13, appellants bring up the Ashkenazi declaration, stating it shows that detection of gene amplification can be used for cancer diagnosis even if the determination includes measurement of aneuploidy. This point is not in question. *If* aneuploidy of the chromosome carrying the PRO809 gene were shown to be associated with cancer in a manner

that would enable its use and support as a substantial assertion its utility as a diagnostic, that would be true. But it has not.

The declaration by Avi Ashkenazi under 37 CFR 1.132 filed 11/3/2004 is insufficient to overcome the rejection under 35 U.S.C. §§101 and 112 because:

It is noted that the declaration is dated 9/15/2003, and was originally submitted in application 09/903,925. It is further noted that the claims in that case are *not* drawn to nucleic acids, but to methods of diagnosis using antibodies that bind to the *protein* encoded by PRO809. It is for this reason (that appellants have been arguing during prosecution the utility of antibodies to protein encoded by the claimed nucleic acids) that much of the Examiner's arguments in the final rejection were directed at utility of the encoded protein. It is relevant that in this application, only amplification of genomic DNA has been measured (however vaguely). There has been no demonstration of mRNA (existence or levels) is it known whether the encoded protein is produced in normal or cancerous cells.

At paragraph 4, declarant states that amplification of certain genes such as HER2/Neu or Myc "gives cancer cells a growth or survival advantage relative to normal cells". No such evidence has been submitted for PRO809, and no activity has been asserted or shown for the protein encoded by PRO809.

At paragraph 5, declarant states that if gene amplification results in over-expression of the mRNA and the corresponding gene product, then it identifies that gene product as a *promising target* for cancer therapy". In the same paragraph, declarant states that "as long as a *significant difference* (emphasis added) relative to normal tissue is detected, it is irrelevant if the signal originates from an increase in the number of gene copies per chromosome and/or an abnormal number of chromosomes." The Examiner agrees with both statements, but finds that with respect to the former statement, there is no evidence of record that the PRO809 gene is transcribed into mRNA at all, nor that such mRNA, if it exists is over-expressed in cancer, nor that the corresponding gene product (protein) is expressed and shows significant differences between cancerous and non-cancerous cells. Further, as discussed above, due to the dearth of information about the "control" samples used, it is not clear that there is a significant difference in PRO809 genomic DNA between cancerous and non-cancerous cells of the sort that would allow use as a diagnostic. Finally, the Declarant's use of the term *promising target* shows that

declarant considers that even if the aforementioned factual requirements were met, that substantial further experimentation would be needed to establish such a use. With respect to the latter point, once again, the Examiner agrees with Declarant's opinion, but does not find that the record supports the assertion that there has been established a significant difference in the sense that there is no correlation possible between the amplification of PRO809 and the likelihood of developing cancer, nor the diagnosis thereof.

Thus, the declaration largely provides declarant opinions, most of which the Examiner agrees with. No data or other evidence are provided, nor any specific information about PRO809 that would serve to support appellants assertions that the data in the specification support as substantial the assertion of utility of the PRO809 nucleic acids for diagnostic use. Finally, the Examiner notes that declarant is an employee of the assignee in this case, and thus has interest in the outcome of these proceedings.

As stated above, the Hittleman reference, discussed at pages 12-13 of the Brief, will not be considered.

At page 13, appellants argue that to overcome the "presumption of truth" that an assertion of utility enjoys that the Examiner must establish that it is "more likely than not" that one of ordinary skill in the art would doubt the truth of the statement of utility. This argument has been fully considered but is not deemed persuasive because appellants are mis-construing the rejection and the Utility Guidelines. The utility guidelines require a specific, substantial and credible assertion of utility. This rejection is on the basis that the asserted utility that PRO809 may be used for the diagnosis of cancer is not substantial. Specificity and credibility are not in question. With regard to whether the asserted utility is substantial, MPEP 2107.01 I.B. clearly states that "Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." The "real world" use being asserted is for the diagnosis of cancer. As argued in the rejection and above, substantial further research would be *required* in order to reasonably confirm that PRO809 could be used in such a manner. Therefore, the assertion of utility is not substantial as defined by the MPEP.

At the paragraph bridging pages 13-14, appellant argues that the *identification* of a diagnostic utility should suffice to provide an "immediate benefit to the public". This argument has been fully considered but is not deemed persuasive because appellants have not identified a diagnostic utility as required by the utility guidelines, but rather have supposed that there *might* be a diagnostic utility, and issued an invitation to perform substantial further research to determine whether or not there is, and if so, for what, and how. Identification of a pharmacological *activity* is *not* comparable to appellant's "identification of a diagnostic utility." 35 U.S.C. §101 requires not only *identification* (assertion) of a utility, but also that that assertion be specific, substantial and credible. The Examiner maintains that the assertion that PRO809 has diagnostic utility is not substantial.

Beginning at page 14, appellants assert that a *prima facie* case of lack of utility has not been established. Appellants argue that the teachings of Hu et al. are not relevant to the instant invention, and that Hu does not "conclusively establish a *prima facie* case for lack of utility." This argument has been fully considered but is not deemed persuasive. First, the Examiner notes that the first office action on the merits did not deal with protein or antibodies at all. It was in response to appellants arguments that the final office action referred to protein and antibodies for establishing utility (sometimes losing sight of the claimed subject matter), for example see the discussion of the Ashkenazi declaration, above. As stated in the final action, , Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than l-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). . By appellants admission, the amplification of the PRO809 genomic DNA is in the 2-3 fold range, well below five-fold Thus, Hu supports, but is not the *basis* of the rejection.

It is noted that all the prior art under consideration appeared in peer-reviewed publications. Appellants repeatedly try to impugn the statistical methods used therein, by

general allegation. The Examiner finds no merit in this argument, with regard to Hu or any other reference.

At pages 15-16, with respect to the Hu reference, appellants again urge that a paper to a particular type of breast tumor cannot be generalized as a principle governing microarray study of breast or other cancers in general. Appellants are urging an improper standard. The Examiner has cited relevant art. *If* art existed to demonstrate facts for PRO809 in particular, she would have cited that, but it does not exist. Therefore, one must turn to the art as a whole for guidance. Appellants try to impugn references for being drawn to different genes than PRO809, or different types of cancers, but have provided no more "relevant", e.g. closer to the instant fact situation, data or references. Accordingly, the record must be judged for what the cited references teach. Hu's "class" of genes provides substantially more evidence than the instant specification. Appellants have pointed to no factual error in the Examiner's conclusion that Hu's paper indicates that genes that are amplified 5-fold or less show no evidence of a correlation between altered gene expression and a known role in disease.

In conclusion, it is noted that M.P.E.P. § 2107 I states:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

In the instant case, the asserted utility that PRO809 nucleic acids are useful as diagnostic markers for cancer is not substantial in that substantial further research is required to reasonably confirm a real world context of use.

At page 17, appellants discuss the standards for determining written description. No comment by the Examiner is necessary.

Appellant argues the art rejection at pages 17 of the Brief. Appellant argues that the Hillier EST clone does not disclose the entire nucleotide sequence of SEQ ID NO: 222, or that their EST was part of a cDNA sequence. The latter point is incorrect. As the person of ordinary skill in the art knows, an EST is an "expressed sequence tag", generated by reverse transcription from mRNA, producing cDNA. As stated in the grounds of rejection, by applicants admission at page 454 of the specification, the clone that was sequenced and designated DNA57836-1338 or PRO809, was purchased from Merck under clone designation H74302. In fact, the specification at page 454 states "the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequence. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 150 and is herein designated DNA57836-1338." The Examiner is at a loss as to how appellants can argue that the sequence that they disclose as having been obtained from a purchased clone can differ from itself. There is no disclosure in the specification of having obtained any additional sequence. Therefore, the Examiner is at a loss as to how there could possibly exist any differences between appellants clone and the one they purchased, as the purchased clone is the *sole* disclosure of how PRO809 was obtained. Any sequence outside the coding region is not relevant, as it is "the full-length coding region" that is being claimed herein. The clone was clearly available from Merck and marketed as a cDNA clone. One of ordinary skill in the art knows that cDNA is generated from mRNA, and thus represents a molecule used by the source cell for making protein (note that this is a distinct situation from those discussed above, in which the Examiner has found that the presence of *genomic* DNA is not predictive of protein). Accordingly, one of ordinary skill in the art purchasing a cDNA clone from Merck would expect that clone to encode one or more proteins. Appellants have repeatedly failed to address this crucial issue, namely that the specification acknowledges that appellants did not isolate the cDNA themselves, but rather bought it from a commercial source. Appellants allege that they have provided an alignment of Hillier's sequence with theirs. However, the Examiner is at a loss as to how the two sequences can possibly be different, as the specification cites Hillier's clone as the source.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Should appellants request an oral hearing before the Board, the Examiner requests to be present.

Respectfully submitted,

Lorraine Spector
Primary Examiner

Conferees:

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER